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ORIGINAL ARTICLE

Persistence with teriparatide in patients with osteoporosis: the UK experience

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Abstract
Introduction The objective of this paper was to determine the persistence with teriparatide at 12 months in all patients in the UK who were prescribed the treatment since its launch.
Methods Virtually all patients prescribed teriparatide in the UK receive treatment through Healthcare at Home, Basingstoke, UK. Data was obtained to assess the start date, discontinuation date and reason for discontinuation in all patients receiving teriparatide since its launch. Persistence was defined as the number of patients continuing treatment.
Results A total of 1,104 patients were included in the analysis. The median duration of use in all patients was 252 days. Of the 435 patients who were at least 12 months post-initiation of treatment, persistence was 87%. Forty-two patients (3.8%) had discontinued treatment due to adverse events.
Conclusions This study demonstrates that persistence with teriparatide at 12 months is very high and is probably greater than that of existing oral therapies for osteoporosis. The reasons for the high persistence rates seen with teriparatide are likely to be multi-factorial. The high persistence rates should help to optimise the effectiveness of therapy in this group of high-risk patients.

Keywords Adverse events · Compliance · Osteoporosis · Persistence · Teriparatide

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Introduction

Osteoporosis is a common systemic disease characterised by low bone mass and micro-architectural deterioration of bone with a consequent increase in the risk of bone fracture. The fractures that result from osteoporosis cause considerable morbidity and mortality, making the disease a major public health problem [1]. The pharmacological agents used most frequently for osteoporosis prevention have proven efficacy, but must be taken long term to be effective. There is, however, evidence of poor adherence and persistence with these therapies, which limit their effectiveness in routine clinical practice. Adherence is defined as "the extent to which a person's behaviour (in terms of taking medications, following diets or executing lifestyle changes) coincides with medical or health advice." Persistence is the duration that the treatment is taken for. Persistence rates at 12 months for oral bisphosphonates have been reported to be as low as 18.5% for daily and 22.1% for weekly users [2, 3]. McCombs et al. [4] report compliance rates below 25% for all osteoporosis therapies using data from a large health insurer of 58,109 osteoporosis patients. A number of studies have shown that, of the women advised to take oestrogen, less than half are still on treatment at one year, with some reporting compliance rates as low as 7% [5, 6]. The major barriers to obtaining good long-term patient persistence for osteoporosis therapies are many and com-

plex, but are likely to include the development of adverse effects and the relative lack of patient education.

Teriparatide is an anabolic agent which, in accordance with NICE (National Institute for Health and Clinical Excellence, England) guidelines, can be prescribed in women over the age of 65 with fragility fractures with extremely low BMDs [7]. It is licensed for a treatment course of 18 months. To the best of our knowledge, no study to date has been conducted in the UK on compliance with teriparatide in the treatment of osteoporosis. In this study, we assessed the persistence with teriparatide in all patients in the UK who had been prescribed the treatment since its launch and had received the drug via Health Care at Home, Basingstoke, England.

Patients and methods

In the UK, Health Care at Home delivers and monitors teriparatide to virtually all patients to whom it is prescribed. The service includes the education of the patients regarding the injection technique, delivery of the medication pens to the patient's home and the collection of all used pens. The returned pens are checked to ensure that the patient is continuing to use the teriparatide and new pens are then issued to those patients deemed to be adherent. This allows a record to be kept of patient persistence. Using the available records provided by Health Care at Home, we were able to access the data of those patients to whom they had provided teriparatide in the UK since its launch. The initial analysis includes 1,104 patients prescribed teriparatide up until February 2006. All patients were prescribed teriparatide by once daily subcutaneous injection at a dose of 20 micrograms per day. A total of 38 patients were excluded from all of the analyses as they died prior to completing treatment.

Data was obtained to assess the start date, discontinuation date and reason for the discontinuation of teriparatide. Persistence was defined as the number of patients continuing treatment. Patients are supplied with three injection pens at a time, which last for a period of 3 months. For this study, we assumed that patients who received their final three pens at 15 months had persisted with treatment until the end of the 18-month course. To facilitate comparisons with studies of bisphosphonates, we defined persistence at 12 months as our primary outcome measure. Demographic data was used to calculate the gender and mean age of the patients. With this data, we were able to investigate whether these patient characteristics predict persistence.

Statistical analysis

Survival analysis was used to model the rate of treatment discontinuation and to estimate the proportion of patients still persisting with treatment at a given time after their start date. All patients were considered to have 'failed' (in a survival analysis context) whenever treatment was discontinued, regardless of whether the discontinuation was due to the 18-month course having been completed or due to drop-out. Thus, if all treatments were completed successfully, the mean length of time to 'failure' would be 18 months. If patients had not 'failed' by the end of the observation period, their data was considered 'censored.' Kaplan-Meier curves were plotted to describe the survival trend of the teriparatide treatment. Predictors of persistence were explored using Kaplen-Meier survival curves and log-rank tests. All statistical analyses were carried out using Stata version 8.2 software.

Results

A total of 1,104 patients were included in the analysis. The median age of the patients was 73.8 years and 91.2% were female. The median duration of use in all 1,104 patients was 252 days. A total of 737 (67%) patients were currently on treatment with teriparatide in the UK, with a median duration of use of 203 days. One hundred and ninety-four patients had completed their 18-month course as planned. Of the 173 patients who had discontinued treatment prematurely, clinician decision was the most common reported reason given (Table 1). Forty-two patients discontinued due to adverse events; although these were not always specified, the most common events reported were: nausea and dizziness (n=8) and headaches (n=6). Seven

Table 1 Descriptive statistics by status at the end of the observation period (N=1,104 with valid data)

Status at end of observation period	N (%)	Median (IQR) time to discontinuation of treatment or end of observation (days)
Current	737 (67%)	203 (111, 365)
Finished: adverse events	42 (3.8%)	124 (67, 226)
Finished: as planned	194 (18%)	548 (548, 548)
Finished: change of drug	5 (0.5%)	253 (206, 385)
Finished: clinician decision	52 (4.7%)	322 (96, 467)
Finished: compliance	3 (0.3%)	230 (202, 245)
Finished: funding	19 (1.7%)	503 (450, 654)
Finished: inadequate response to treatment	7 (0.6%)	295 (190, 396)
Finished: no reason	4 (0.4%)	118 (73, 203)
Finished: patient request	41 (3.7%)	217 (51, 455)
Total	1,104 (100%)	263 (126, 476)

IQR=Inter-quartile range

patients did not complete their treatment due to an inadequate response.

The Kaplan-Meier survival curves for cumulative persistence with therapy are shown in Fig. 1. A total of 704 patients had reached 6 months at the time the data was available and the proportion persisting with therapy was 93%. At 12 months, 87% out of a total of 435 patients were persisting with therapy. 79% out of a total of 237 persisted with the prescribed 18-month course. A total of 43 patients continued to use teriparatide beyond 18 months (Fig. 1). Neither age nor gender predicted persistence with therapy.

Discussion

To the best of our knowledge, the present study is the first to have assessed persistence with teriparatide since its launch in the UK. The results from our study indicate that persistence with teriparatide in clinical practise is high, with 87% of patients on treatment for 12 months still on treatment. These results are very favourable when compared with persistence rates for the conventional treatment of osteoporosis with daily or weekly oral bisphosphonates.

Previous studies have found that only around 50–60% of patients are compliant with their treatment across a range of chronic diseases [8], and that patients who are poorly compliant have significantly more adverse outcomes. Previous studies of persistence with oral bisphosphonates have demonstrated variable persistence rates. Data from two large US studies using health care organisations, which include all patients prescribed bisphosphonates, have provisionally reported 12-month persistence rates of 18.5% and 22.1% for daily bisphosphonates. The rates for weekly bisphosphonates, although higher at 31.7% and 44.2%, respectively, still leave considerable room for improvement [2, 3]. Comparisons of persistence and compliance for different osteoporosis treatments should ideally be made against weekly bisphosphonates due to the general move towards their prescription. Data from tertiary referral centres, which contain highly selected patients within a specialised service, often including educational programmes and regular follow-up, have demonstrated higher persistence rates of up to 77.6% for daily alendronate and 90.3% for etidronate [9]. These results are similar to the results obtained in this study. It is probable that the setting in which the patient is prescribed osteoporosis therapy is an important determinant of persistence. We therefore attempted to ascertain the origin of the prescription for each of our patients. Although our dataset is not formally set up to examine the type of referral centre, we identified the hospital that prescribed the teriparatide for each patient. From this data, it is estimated that less than one third of patients were prescribed teriparatide by a tertiary referral centre, the majority originating from District General hospitals.

There are a number of factors that influence a patient's decision to persist with treatment, some of which may be relevant in our group of patients: for example, the balance of benefit versus risk of side effects, education and regular follow-up, inconvenience of the treatment regime and the financial implications in those treated in the private health care sector. To be eligible for teriparatide under the NICE guidance, patients must have already sustained several fractures, have failed or been intolerant to a bisphospho-

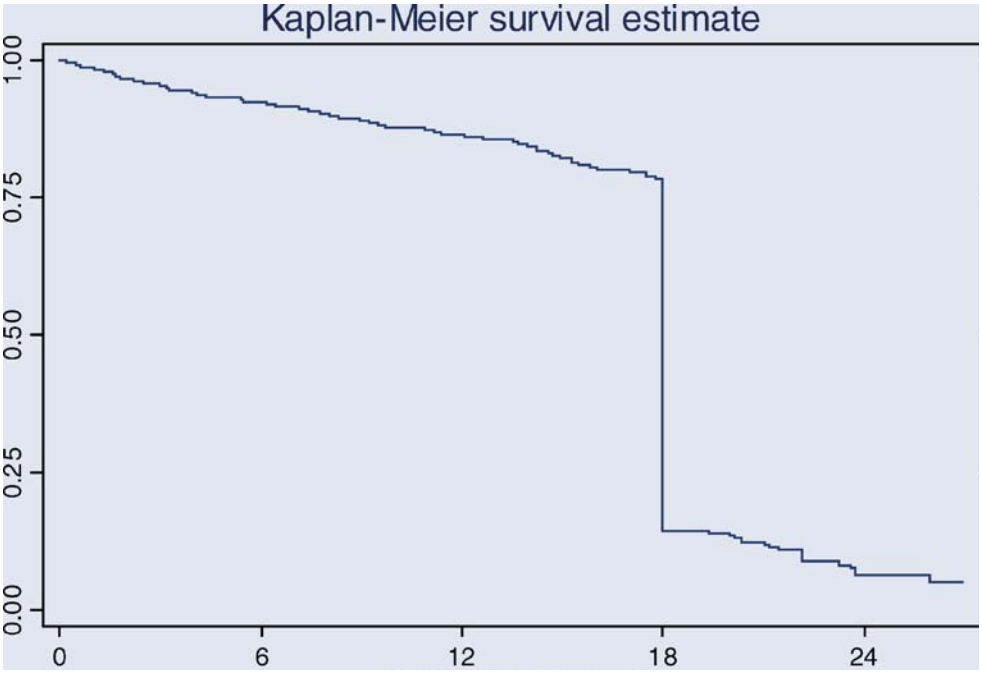

Fig. 1 Kaplan-Meier survival curve for teriparatide treatment

nates and to have the drug prescribed by a specialist. These patients will, therefore, be a severe group of patients who have failed several therapies and will often suffer considerable pain and, hence, will probably perceive a greater benefit-to-risk ratio than most patients prescribed other osteoporosis treatments in primary care, which may increase persistence. These patients may have received more information and education with regards to their illness and the treatment from their specialist and during the nurse training sessions provided at the initiation of therapy, which may have increased persistence rates. Regular review by the service provider may also be important in increasing persistence with treatment; a previous study has demonstrated that regular review by a nurse can increase adherence by 57% and persistence by 25% [10].

Our study group of patients may have suffered previous adverse events with first-line treatments for osteoporosis and this may have led to stopping treatment. Indeed, several studies have reported adverse events occurring in 31–38% of patients on treatment with bisphosphonates and this resulted in 20% of patients discontinuing treatment in some studies [11, 12]. In our study, adverse events only led to discontinuation in 3.8% of patients, suggesting that the treatment is generally well tolerated, which may be an important contributing factor in patient persistence. However, it is also possible that this group of patients with severe disease were more willing to tolerate side-effects than patients in other studies. Finally, patients may have preferred the administration route of the drug, since it is given by a once-daily subcutaneous injection, as opposed to the regime required for oral bisphosphonates. We were interested to see that a number of patients continued therapy beyond the licensed duration of 18 months. Unfortunately, we did not have access to the reasons for these decisions.

A limitation of our study was that persistence for the last 3 months of treatment was not measured directly, but was based on the continuing supply of the pens for administration of the treatment; we have, therefore, made the assumption that these patients were persistent. These results are specific to the United Kingdom, where teriparatide is administered through Healthcare at Home with its package of education and regular nurse led follow-up, and cannot necessarily be extrapolated to other healthcare systems with different methods of administration. We had little additional information available on the reasons for discontinuation other than the categories presented. Although it would have been very interesting to have further details, their absence does not affect the primary outcome or objectives of this study.

In conclusion, this study demonstrates that persistence with teriparatide at 12- and 18-months treatment is very high and probably greater than that of existing oral therapies for osteoporosis. The reasons for high compliance are multi-factorial and should help to optimise the effectiveness of therapy in this group of high-risk patients.

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